

CLAIMS

What is claimed is:

1. An isolated antibody that specifically binds to an epitope specifically bound by an antibody expressed by a clone selected from the group consisting of clone S25,
5 clone C25, clone C39, clone 1C6, clone 3D12, clone B4, clone 1F3, clone huC25, clone Ar1, clone Ar2, clone WR1(V), clone WR1(T), clone 3-1, clone 3-8, clone 3-10, and clone ING1, wherein said antibody binds to and neutralizes botulinum neurotoxin type A (BoNT/A).
2. The antibody of claim 1, wherein said clone is S25.
3. The antibody of claim 1, wherein said clone is C25 or C39.
- 10 4. The antibody of claim 1, wherein said clone is 1C6.
5. The antibody of claim 1, wherein said clone is 1F3.
6. The antibody of claim 1, wherein said clone is 3D12.
7. The antibody of claim 1, wherein said clone is B4.
8. The antibody of claim 1, wherein said clone is huC25.
- 15 9. The antibody of claim 1, wherein said clone is Ar1.
10. The antibody of claim 1, wherein said clone is Ar2.
11. The antibody of claim 1, wherein said clone is WR1(V).
12. The antibody of claim 1, wherein said clone is WR1(T).
13. The antibody of claim 1, wherein said clone is 3-1.
- 20 14. The antibody of claim 1, wherein said clone is 3-8.
15. The antibody of claim 1, wherein said clone is 3-10.
16. The antibody of claim 1, wherein said clone is ING1.

17. The antibody of claim 1, wherein said antibody comprises at least two variable heavy (V_H) complementarity determining regions (CDRs) listed in Table 4, Table 9, or Table 11.

18. The antibody of claim 17, wherein said antibody comprises at three 5 variable heavy (V_H) complementarity determining regions (CDRs) listed in Table 4, Table 9, or Table 11.

19. The antibody of claim 1, wherein said antibody further comprises a variable light (V_L) complementarity determining region (CDR) listed in Table 4, Table 9, or Table 11.

10 20. The antibody of claim 19, wherein said antibody comprises at least two variable light (V_L) complementarity determining regions (CDRs) listed in Table 4, Table 9, or Table 11.

15 21. The antibody of claim 20, wherein said antibody comprises three variable light (V_L) complementarity determining regions (CDRs) listed in Table 4, Table 9, or Table 11.

22. The antibody of claim 1, wherein said antibody is an antibody expressed by a clone selected from the group consisting of a clone listed in Table 4, Table 9, or Table 11.

20 23. The antibody of claim 1, wherein said antibody is a single chain Fv (scFv).

24. The antibody of claim 1, wherein said antibody is an IgG.

25. The antibody of claim 1, wherein said antibody is a Fab.

26. The antibody of claim 1, wherein said antibody is a $(Fab')_2$.

27. The antibody of claim 1, wherein said antibody is a $(scFv')_2$.

25 28. The antibody of claim 27, wherein said antibody is a fusion protein of two scFv fragments.

29. The antibody of claim 1, wherein said antibody comprises a framework region listed in Table 4, Table 9, or Table 11.

30. The antibody of claim 29, wherein said framework is a variable heavy (V_H) frame work region listed in Table 4, Table 9, or Table 11.

5 31. The antibody of claim 29, wherein said framework is a variable light (V_L) frame work region listed in Table 4, Table 9, or Table 11.

32. The antibody of claim 30, wherein said antibody comprises at least two variable heavy (V_H) framework regions listed in Table 4, Table 9, or Table 11.

10 33. The antibody of claim 31, wherein said antibody comprises at least two variable light (V_L) framework regions listed in Table 4, Table 9, or Table 11.

34. The antibody of claim 30, wherein said antibody comprises a variable heavy (V_H) region listed in Table 4, Table 9, or Table 11.

35. The antibody of claim 31, wherein said antibody comprises a variable light (V_L) region listed in Table 4, Table 9, or Table 11.

15 36. An isolated anti-botulinum neurotoxin type A (anti-BoNT/A) antibody, said antibody comprising a variable heavy (V_H) complementarity determining region (CDR) listed in Table 4, Table 9, or Table 11, and wherein said antibody specifically binds to and neutralizes a botulinum neurotoxin type A.

20 37. The antibody of claim 36, wherein said antibody binds both an A1 and an A2 toxin.

38. The antibody of claim 36, wherein said antibody comprises at least two variable heavy (V_H) complementarity determining regions (CDRs) listed in Table 4, Table 9, or Table 11.

25 39. The antibody of claim 38, wherein said antibody comprises at three variable heavy (V_H) complementarity determining regions (CDRs) listed in Table 4, Table 9, or Table 11.

40. The antibody of claim 36, wherein said antibody further comprises a variable light (V_L) complementarity determining region (CDR) listed in Table 4, Table 9, or Table 11.

5 41. The antibody of claim 40, wherein said antibody comprises at least two variable light (V_L) complementarity determining regions (CDRs) listed in Table 4, Table 9, or Table 11.

42. The antibody of claim 41, wherein said antibody comprises three variable light (V_L) complementarity determining regions (CDRs) listed in Table 4, Table 9, or Table 11.

10 43. The antibody of claim 36, wherein said antibody is an antibody expressed by a clone selected from the group consisting of a clone listed in Table 4, Table 9, or Table 11.

44. The antibody of claim 36, wherein said antibody is an IgG.

15 45. The antibody of claim 36, wherein said antibody is a single chain Fv (scFv).

46. The antibody of claim 36, wherein said antibody is a Fab.

47. The antibody of claim 36, wherein said antibody is a (Fab')₂.

48. The antibody of claim 36, wherein said antibody is a (scFv')₂.

20 49. The antibody of claim 48, wherein said antibody is a fusion protein of two scFv fragments.

50. The antibody of claim 36, wherein said antibody comprises a framework region listed in Table 4, Table 9, or Table 11.

51. The antibody of claim 50, wherein said framework is a variable heavy (V_H) frame work region listed in Table 4, Table 9, or Table 11.

25 52. The antibody of claim 50, wherein said framework is a variable light (V_L) frame work region listed in Table 4, Table 9, or Table 11.

53. The antibody of claim 51, wherein said antibody comprises at least two variable heavy (V_H) framework regions listed in Table 4, Table 9, or Table 11.

54. The antibody of claim 52, wherein said antibody comprises at least two variable light (V_L) framework regions listed in Table 4, Table 9, or Table 11.

5 55. The antibody of claim 51, wherein said antibody comprises a variable heavy (V_H) region listed in Table 4, Table 9, or Table 11.

56. The antibody of claim 52, wherein said antibody comprises a variable light (V_L) region listed in Table 4, Table 9, or Table 11.

10 57. The antibody of claim 36, wherein antibody specifically binds to an epitope specifically bound by an antibody expressed by a clone selected from the group consisting of clone S25, clone C25, clone C39, clone 1C6, clone 3D12, clone B4, clone 1F3, clone huC25, clone Ar1, clone Ar2, clone WR1(V), clone WR1(T), clone 3-1, clone 3-8, clone 3-10, and clone ING1.

15 58. A method of neutralizing a botulinum neurotoxin type A (BoNT/A), said method comprising contacting said botulinum neurotoxin type A with a first anti-botulinum neurotoxin type A (anti-BoNT/A) antibody, said antibody comprising a variable heavy (V_H) complementarity determining region (CDR) listed in Table 4, Table 9, or Table 11 said antibody having a specificity and affinity such that it specifically binds to binds to and neutralizes said botulinum neurotoxin type A.

20 59. The method of claim 58, wherein said antibody binds both an A1 and an A2 toxin.

25 60. The method of claim 58, further comprising contacting said botulinum neurotoxin type A with a second anti-botulinum neurotoxin type A (anti-BoNT/A) antibody, said antibody comprising a variable heavy (V_H) complementarity determining region (CDR) listed in Table 4, Table 9, or Table 11, said antibody having a specificity and affinity such that it specifically binds to binds to and neutralizes said botulinum neurotoxin type A, wherein said second anti-botulinum neurotoxin type A (anti-BoNT/A) antibody binds to a different epitope than said first anti-botulinum neurotoxin type A (anti-BoNT/A) antibody.

61. The method of claim 58, wherein said antibody comprises at least two variable heavy (V_H) complementarity determining regions (CDRs) listed in Table 4, Table 9, or Table 11.

5 62. The method of claim 61, wherein said antibody comprises at three variable heavy (V_H) complementarity determining regions (CDRs) listed in Table 4, Table 9, or Table 11.

63. The method of claim 58, wherein said antibody further comprises a variable light (V_L) complementarity determining region (CDR) listed in Table 4, Table 9, or Table 11.

10 64. The method of claim 63, wherein said antibody comprises at least two variable light (V_L) complementarity determining regions (CDRs) listed in Table 4, Table 9, or Table 11.

15 65. The method of claim 64, wherein said antibody comprises three variable light (V_L) complementarity determining regions (CDRs) listed in Table 4, Table 9, or Table 11.

66. The method of claim 58, wherein said antibody is an antibody expressed by a clone listed in Table 4, Table 9, or Table 11.

67. The method of claim 58, wherein said antibody is an IgG.

68. The method of claim 58, wherein said antibody is a single chain Fv

.20 (scFv).

69. The method of claim 58, wherein said antibody is a Fab.

70. The method of claim 58, wherein said antibody is a (Fab')₂.

71. The method of claim 58, wherein said antibody is a (scFv')₂.

72. The method of claim 71, wherein said antibody is a fusion protein of
25 two scFv fragments.

73. The method of claim 58, wherein said antibody comprises a framework region listed in Table 4, Table 9, or Table 11.

74. The method of claim 73, wherein said framework is a variable heavy (V_H) frame work region listed in Table 4, Table 9, or Table 11.

75. The method of claim 73, wherein said framework is a variable light (V_L) frame work region listed in Table 4, Table 9, or Table 11.

5 76. The method of claim 74, wherein said antibody comprises at least two variable heavy (V_H) framework regions listed in Table 4, Table 9, or Table 11.

77. The method of claim 75, wherein said antibody comprises at least two variable light (V_L) framework regions listed in Table 4, Table 9, or Table 11.

10 78. The method of claim 74, wherein said antibody comprises a variable heavy (V_H) region listed in Table 4, Table 9, or Table 11.

79. The method of claim 75, wherein said antibody comprises a variable light (V_L) region listed in Table 4, Table 9, or Table 11.

15 80. A polypeptide comprising botulinum neurotoxin type A (BoNT/A) neutralizing epitope, said neutralizing epitope comprising an epitope specifically bound by an antibody expressed by a clone selected from the group consisting of clone S25, clone C25, clone C39, clone 1C6, clone 3D12, clone B4, clone 1F3, clone huC25, clone Ar1, clone Ar2, clone WR1(V), clone WR1(T), clone 3-1, clone 3-8, clone 3-10, and clone ING1, wherein said polypeptide is not a full-length botulinum neurotoxin H_c fragment.

20 81. The polypeptide of claim 80, wherein said polypeptide is a fragment of BoNT/A H_C having a length of at least 8 amino acids.

82. The polypeptide of claim 80, wherein said clone is S25.

83. The polypeptide of claim 80, wherein said clone is C25 or C39.

84. The polypeptide of claim 80, wherein said clone is 1C6.

85. The polypeptide of claim 80, wherein said clone is 1F3.

25 86. The antibody of claim 80, wherein said clone is 3D12.

87. The antibody of claim 80, wherein said clone is B4.

88. The antibody of claim 80, wherein said clone is huC25.
 89. The antibody of claim 80, wherein said clone is Ar1.
 90. The antibody of claim 80, wherein said clone is Ar2.
 91. The antibody of claim 80, wherein said clone is WR1(V).
 - 5 92. The antibody of claim 80, wherein said clone is WR1(T).
 93. The antibody of claim 80, wherein said clone is 3-1.
 94. The antibody of claim 80, wherein said clone is 3-8.
 95. The antibody of claim 80, wherein said clone is 3-10.
 96. The antibody of claim 80, wherein said clone is ING1.
- 10 97. A method of making a botulinum neurotoxin type A antibody (anti-BoNT/A) that neutralizes BoNT/A, said method comprising:
 contacting a plurality of antibodies with a epitope specifically bound by an antibody expressed by a clone selected from the group consisting of clone S25, clone C25, clone C39, clone 1C6, clone 3D12, clone B4, clone 1F3, clone huC25, clone Ar1,
15 clone Ar2, clone WR1(V), clone WR1(T), clone 3-1, clone 3-8, clone 3-10, and clone ING1;
 and
 isolating an antibody that specifically binds to said epitope.
98. The method of claim 97, wherein said clone is S25.
 99. The method of claim 97, wherein said clone is C25 or C39.
 - 20 100. The method of claim 97, wherein said clone is 1C6.
 101. The method of claim 97, wherein said clone is 1F3.
 102. The antibody of claim 97, wherein said clone is 3D12.
 103. The antibody of claim 97, wherein said clone is B4.
 104. The antibody of claim 97, wherein said clone is huC25.

105. The antibody of claim 97, wherein said clone is Ar1.
106. The antibody of claim 97, wherein said clone is Ar2.
107. The antibody of claim 97, wherein said clone is WR1(V).
108. The antibody of claim 97, wherein said clone is WR1(T).
- 5 109. The antibody of claim 97, wherein said clone is 3-1.
110. The antibody of claim 97, wherein said clone is 3-8.
111. The antibody of claim 97, wherein said clone is 3-10.
112. The antibody of claim 97, wherein said clone is ING1.
113. The method of claim 97, wherein said plurality of antibodies are
10 antibodies displayed on a surface protein of a phage.
114. The method of claim 97, wherein said plurality of antibodies are
antibodies in serum from a mammal.
115. The method of claim 97, wherein said plurality of antibodies are
antibodies expressed by hybridomas.
- 15 116. A composition comprising a plurality of anti-botulinum neurotoxin
antibodies, wherein each antibody is specific for a different epitope of a botulinum
neurotoxin, and wherein said combination of antibodies shows greater toxin neutralization
than the single antibodies comprising said plurality.
117. The composition of claim 116, wherein said composition comprises a
20 first antibody that binds and neutralizes an A1 toxin and a second antibody that binds and
neutralizes an A2 toxin.
118. A method of neutralizing a botulinum neurotoxin, said method
comprising contacting said neurotoxin with a plurality of anti-botulinum neurotoxin
antibodies, wherein each antibody is specific for a different epitope of said botulinum
25 neurotoxin, and wherein said combination of antibodies shows greater toxin neutralization
than the single antibodies comprising said plurality.